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EXAMINER	
KIM, YOUNG J	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 05/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/901,181	BURG ET AL.	
	Examiner	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/21/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The present Office Action is responsive to the Amendment received on February 15, 2006.

Preliminary Remark

Claims 1 and 2-9 are canceled.

Claims 10-36 are pending and are under prosecution.

The present Office Action contains at least one rejection not necessitated by Amendment, and therefore, is made **Non-Final.**

Information Disclosure Statement

The IDS received on December 21, 2005 is received with the fee under 37 CFR 1.17(p).

A signed copy of the PTO-1449 is enclosed herewith.

Claim Rejections - 35 USC § 112

The rejection of claims 31, 33, and 34 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter, made in the Office Action mailed on October 13, 2005, is withdrawn in view of the Amendment received on February 15, 2006.

Rejection, Maintained

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 15, 16[1], and 24 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter, made in the Office Action mailed on October 13, 2005 is maintained for the reasons of record.

Applicants contend that the amendment made to claim 10 overcomes the rejection and renders the rejection moot (page 6, 2nd paragraph, Response).

The amendment, however, does not overcome the rejection as explained below.

Claim 15 has been amended to recite that "said apparatus transfer said product from said first reaction vessel to a second reaction vessel **containing said nucleic acid amplification enzyme**." Hence, claim 15 requires that that the second reaction vessel already contain the nucleic acid amplification enzyme.

However, its parent claim, claim 10(d), recites that the "product from said first reaction vessel" is contacted with "a nucleic acid amplification enzyme, **then** amplified in a second reaction vessel.

Hence, it becomes unclear whether the nucleic acid amplification enzyme is present in the second reaction vessel in addition to that which was already added in the first reaction vessel, or whether the claim 10(d) is erroneous in stating that the nucleic acid enzyme is added in the first reaction vessel.

Clarification is requested.

Claim 16 recites that the apparatus transfers said nucleic acid amplification enzyme contained in said second reaction vessel. However, claim 10 recite that the nucleic acid amplification enzyme is added to the first nucleic acid **prior** to the transference to the second

[1] The previous Office Action contained a typographical error on page 3, 2nd paragraph. The phrase which was recited as being indefinite was typographically stated as being present in claim 15. However, it is apparent that claim 16 is the claim which contained the indefinite phrase. The rejection is maintained herein.

reaction vessel. Thus, there lacks any antecedent basis that the amplification enzyme is present in the second reaction vessel.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 10, 11, 14-16, 21-25, 27, and 30-35 are rejected under 35 U.S.C. 102(e) as being anticipated by Lipshutz et al. (U.S. Patent No. 5,856,174, issued January 5, 1999, filed January 19, 1996, priority June 29, 1995).

Lipshutz et al. disclose a method of detecting the presence or absence of a single stranded or double stranded first nucleic acid in a sample (i.e., diagnostic assay; see column 4, line 38).

Lipshutz et al. employ a microfluidic device which comprises a plurality of chambers (or vessels), wherein each chamber is fluidically connect to one another (column 2, lines 21-26; thus in fluid communication with each other).

Lipshutz et al. employ this microfluidic device for target nucleic acid detection, wherein the method comprises:

a) combining in a first reaction chamber (or vessel); a test sample and reagents suitable for carrying out a nucleic acid amplification reaction such that a reaction mixture can form and placing said reaction chamber (column 6, lines 29-31 and 38-42) in an automated apparatus (column 4, lines 16-21; computerized, thus automated) such that;

b) the automated apparatus heats said first reaction vessel to a sufficient temperature (column 7, line 16) to render any double stranded first nucleic acid in the sample to be tested into sufficient single stranded nucleic acid (or "denaturation"), and

c) the automated apparatus cools said first reaction chamber to a sufficient temperature to form a hybridization product, said hybridization product comprising at least one oligonucleotide primer and a first nucleic acid (or "hybridization" of the primer to the template, see column 6, lines 57-60; column 6, line 67),

d) contacting said product in the first reaction chamber with a nucleic acid amplification enzyme (column 8, lines 23-25),

e) amplifying the first nucleic acid in the amplification chamber (column 8, lines 1-3); and

f) detecting the presence of the amplicons (column 11, lines 43-52).

While the artisans explicitly disclose that the primer hybridization, denaturation and annealing of the primer in the amplification reaction for PCR aspect, the artisans are also explicit in stating that isothermal amplification such as LCR is also used for amplification, thereby clearly anticipating claims 10 and 27.

With regard to claim 11, the detection of the amplified product is disclosed as being achieved on an array of oligonucleotides (column 9, lines 30-35), thus capture probe bound on a solid support.

With regard to claims 14 and 30, the reagents involved in amplification is disclosed as comprising buffer, dNTPs, or at least one primer (column 7, lines 11 and 52). It should also be noted that LCR (known as Ligation Chain Reaction, involves primers, enzymes, and nucleotides).

With regard to claim 15, the amplification is performed in a second chamber containing an amplification enzyme (i.e., pre-dosed) (column 8, lines 2-3).

With regard to claims 16, 24, and 34, the amplification enzyme is, in the alternative, delivered to the first reaction chamber for amplification (column 8, lines 3-6; thus during the transfer process).

With regard to claims 21 and 32, the microfluidic device is disclosed as having a detection device which allows the detection of the labeled nucleic acid products (column 11, lines 45-52).

With regard to claims 22 and 33, the amplification reagents are disclosed as being pre-dosed (column 8, line 17) in lyophilized form (column 8, line 19).

With regard to claim 23, the amplification reaction chamber is disclosed as being "sealable" (column 7, lines 65-66), which implies that the chamber would be "sealed."

With regard to claims 25, 31, and 35, each chamber is fluidically connected to each other (column 2, lines 21-26), wherein the fluid flow is controlled by a valve (column 2, lines 62-67; thus transporting).

Therefore, Lipshutz et al. clearly anticipate the invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 12, 13, 19, 20, and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lipshutz et al. (U.S. Patent No. 5,856,174, issued January 5, 1999, filed January 19, 1996, priority June 29, 1995) in view of Mandrand et al. (U.S. Patent No. 5,695,936, issued December 9, 1997, priority June 14, 1995).

The teachings of Lipshutz et al. have already been discussed above.

Lipshutz et al. do not explicitly disclose that the capture probe hybridization complex (the hybridization complex formed between the amplicons and the capture probe) is contacted with a labeled nucleic acid probe specific for the amplicons (claims 12 and 29) to form a labeled probe complex, and that the labeled probe complex is contacted with a substrate to generate a detectable label (claim 13).

Lipshutz et al. are do not explicitly disclose that the capture probe hybridization complex bound on the solid support is washed so as to remove the non-specific hybridization (claim 19) and that the labeled probe complex is washed so as to remove the non-specifically bound amplicons and labeled nucleic acid probes from the solid support (claim 20).

Mandrand et al. disclose a well known method of detecting nucleic acid hybridization on a solid substrate, wherein the solid substrate (microtitre plate) comprises a plurality of immobilized oligonucleotide probes (column 15, lines 18-24) and wherein the artisans state that the hybridization complex formed between the immobilized oligonucleotide probes in the microtitre plate (or capture probes; column 15, lines 27-33) and the target nucleic acid is detected by a set of detector probes which are complementary to the portion of the target nucleic acid (see Figure 1; column 15, lines 35-40).

The detector probe is disclosed as being labeled with alkaline phosphatase (column 15, lines 35-36), thereby meeting the limitation of claims 12 and 29.

With regard to claim 13, Mandrand et al. explicitly disclose that the labeled probe complex is contacted with a substrate (or PNPP, para-nitrophenyl phosphate, a substrate of the alkaline phosphatase; column 16, lines 2-16).

With regard to claim 19, Mandrand et al. explicitly disclose a well known method of washing the complex formed between the immobilized oligonucleotides (or capture probes) and the target nucleic acid, for the purpose of removing non-specific hybridization (column 15, line 34).

With regard to claim 20, Mandrand et al. explicitly disclose a well-known method of washing the complex formed between the target nucleic acid with the detector probe, for the purpose of removing non-specifically bound detector probe (column 15, lines 42-44).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Lipshutz et al. with the teachings of Mandrand et al., thereby arriving at the invention as claimed for the following reasons.

The step of washing hybridization complexes, the complexes of which are formed between the immobilized probe and the target; or the complex formed from the immobilized probe, target, and the detector probe, is a common practice in the art of nucleic acid hybridization. Such wash step ensures that non-specifically bound target nucleic acids or the detector probes are washed away, precluding false-positive results.

While Lipshutz et al. are not explicit in discussing this knowledge, Mandrand et al. clearly evidences that the practice had been well established at the time the invention was made. Hence, one of ordinary skill in the art at the time the invention was made would have been motivated to employ the washing steps of Mandrand et al. in the method of Lipshutz et al., for the advantage of reducing false-positive outcomes.

With regard to the embodiments drawn to the substrate-mediated detection, one of ordinary skill in the art would have been motivated to employ any of the well-known means of detection, such as direct labeling of the target nucleic acid (or amplicons), labeled detector probe (of Mandrand

et al.), etc. as such detection techniques had been well-established, giving said one of ordinary skill in the art a reasonable expectation of success at combining the teachings.

MPEP, at 2143.02, states that the prior art can be modified or combined to reject claims as obvious as long as there is a reasonable expectation of success.

Therefore, for the above reasons, the invention as claimed is *prima facie* obvious over the cited references.

Claims 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lipshutz et al. (U.S. Patent No. 5,856,174, issued January 5, 1999, filed January 19, 1996, priority June 29, 1995) in view of Mabilat et al. (Journal of Clinical Microbiology, November 1994, vol. 32, no. 11, pages 2702-2705; IDS ref# 47[2]).

The teachings of Lipshutz et al. have already been discussed above.

Lipshutz et al. do not explicitly disclose that the solid support comprising the capture probes is a pipette-like device (claim 17), wherein said solid support is controlled by an automated apparatus (claim 18).

Mabilat et al. disclose a detection apparatus which is automated, wherein the detection apparatus comprise a solid support in the form of a pipette-like shape (see Figure 1), wherein said solid support comprises a capture probe for target nucleic acids (page 2703, 1st column, bottom paragraph; in the phrase, "[o]ne oligonucleotide was applied as a coating inside the solid surface of the pipette tip, the solid phase receptacle (SPR), and acted as a capture probe").

The automated apparatus of Mabilat et al. allows the pipette tip comprising the capture probe to scan across a series of wells for conducting different parts of the steps involved in hybridization reaction (see Figure 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Lipshutz et al. and Mabilat et al., thereby arriving a the claimed invention for the following reasons.

Lipshutz et al. disclose a microfluidic device which comprises a plurality of chambers which are fluidically connected. The artisans explicitly state that different reactions could be conducted in each of the chambers, wherein the product of a particular chamber is fluidically transferred to the next chamber for a variety of different reactions (column 4, lines 25-29).

Mabilat et al. explicitly disclose that their detection device allows nucleic acid hybridization detection in 2 hrs, wherein the detection is completely automated.

Given such an advantage, one of ordinary skill in the art at the time the invention was made would have been motivated to combine the detection device of Mabilat et al. with the device of Lipshutz et al., thereby arriving at a method of using an integrated device which allows sample preparation, such as isothermal amplification reaction, and detection in a facilitated and automated manner.

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

Claims 26 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lipshutz et al. (U.S. Patent No. 5,856,174, issued January 5, 1999, filed January 19, 1996, priority June 29, 1995) in view of in view of Fanning et al. (U.S. Patent No. 5,762,873, issued June 9, 1998, filed February 21, 1996).

The teachings of Lipshutz et al. have already been discussed above.

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[2] IDS received on February 7, 2005.

Lipshutz et al., while explicitly disclosing that "[a] variety of microvalve designs are particularly well suited for their device," do not explicitly suggest a thimble valve (claims 26 and 36).

Fanning et al. disclose a device which comprises thimble valves for the purpose of controlling the fluid flow.

MPEP, at 2143.02, states that the prior art can be modified or combined to reject claims as obvious as long as there is a reasonable expectation of success. Given that thimble valve had been well known and established in the art for controlling fluid flow, one of ordinary skill in the art at the time the invention was made would have had a clear expectation of success at combining the teachings of Lipshutz et al. with the teachings of Fanning et al, thereby arriving at the invention as claimed.

Therefore, for the above reasons, the invention as claimed is *prima facie* obvious over the cited references.

Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lipshutz et al. (U.S. Patent No. 5,856,174, issued January 5, 1999, filed January 19, 1996, priority June 29, 1995) in view of in view of Nadeau et al. (U.S. Patent No. 5,457,027, issued October 10, 1995; IDS ref# 4[2]).

The teachings of Lipshutz et al. have already been discussed above.

Lipshutz et al., while explicit in disclosing that isothermal amplification is conducted in a chamber of their device, are not explicit in stating that an internal control is employed in the amplification reaction (claim 28).

Nadeau et al. disclose a method of employing internal control in a method of isothermal amplification for the advantage of determining the efficacy of the amplification reaction (column 5, lines 4-5) and to quantity the pre-amplification target levels (column 5, lines 6-7).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to employ the teachings of Nadeau et al. in an isothermal amplification reaction of Lipshutz et al., thereby arriving at the claimed invention for the following reasons.

By employing an internal control for amplification reaction, particularly for isothermal amplification, one of ordinary skill in the art would have been capable of determining the initial amount of target nucleic acid present in the sample prior to amplification, the determination of which would be of significant importance (i.e., motivation) in bacterial or viral diagnosis.

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

Double Patenting – Maintained

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The rejection of claims 10, 14-16, and 21-24 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of the U.S. Patent No. 6,300,068 made in the Office Action mailed on October 13, 2005 is maintained for the reasons of record.

The rejection of claims 11-13 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of the U.S. Patent No. 6,300,068 in view of

Backus et al. (U.S. Patent No. 6,280,930), made in the Office Action mailed on October 13, 2005 is maintained for the reasons of record.

The rejection of claims 11 and 17 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of the U.S. Patent No. 6,300,068 in view of Backus et al. (U.S. Patent No. 6,280,930) and Harris et al. (U.S. Patent No. 5,849,544) made in the Office Action mailed on October 13, 2005 is maintained for the reasons of record.

The rejection of claims 19-20 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of the U.S. Patent No. 6,300,068 in view of Collins et al. (U.S. Patent No. 6,268,128) made in the Office Action mailed on October 13, 2005 is maintained for the reasons of record.

The rejection of claims 27-36 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,300,068, made in the Office Action mailed on October 13, 2005 is maintained for the reasons of record.

Applicants state that a terminal disclaimer will be filed upon indication of allowable claims. Since a properly terminal disclaimer has not been filed to date, the rejection is maintained.

Conclusion

No claims are allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner is on flex-time schedule and can best be reached from 8:30 a.m. to 4:30 p.m. The Examiner can also be reached via e-mail to Young.Kim@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary Benzion, can be reached at (571) 272-0782.

Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (571) 273-8300. For Unofficial documents, faxes can be sent directly to the Examiner at (571) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Young J. Kim
Patent Examiner
Art Unit 1637
5/5/2006

YOUNG J. KIM
PATENT EXAMINER

yjk